

## A case of fatal peri-partum cardiomyopathy

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*A case of fatal cardiomyopathy presenting in the puerperium is described. Despite extensive investigation and post-mortem examination no aetiological factor was found. The diagnosis of specific peri-partum cardiomyopathy is discussed.*

The existence of a syndrome of peri-partum cardiomyopathy is controversial. The earliest significant reports of myocardial disease in pregnancy and the puerperium were from Gouley, McMillan, and Bellet (1937) and Hull and Hafkesbring (1937), and further reports were reviewed by Meadows (1957, 1960). Benchimol, Carneiro, and Schlesinger (1959) were able to identify toxæmia, hypertension, or a specific myocarditis as the causes of their cases of post-partum heart disease.

We accept Bridgen's (W. Bridgen, 1969, personal communication) term peri-partum cardiomyopathy, because some cases present before, others after delivery. We define this as primary myocardial disease occurring for the first time in the last trimester of pregnancy or the first trimester after delivery in the absence of pre-eclamptic toxæmia, hypertension, or any other known heart disease. If all cases without previous documented medical examinations, all cases with hypertension and albuminuria, and all cases with a significant infective illness are excluded, only 2 fully documented cases have been described in white women (Case 2 of Brown *et al.*, 1967; Muller and Bonard, 1968). Four further cases have been mentioned in reviews (Bridgen, 1957; Goodwin *et al.*, 1961).

Less rigidly defined post-partum heart disease has been reported frequently in negroes (Meadows, 1960; Seftel and Susser, 1961; Pierce, Price, and Joyce, 1963; Walsh *et al.*, 1965; Stuart, 1968) and also in Ceylonese (Nagaratnam and Somasundram, 1965) and Saudi-Arabians (Perrine, 1967).

The present case fulfilled the diagnostic

criteria for peri-partum cardiomyopathy, and provides further evidence for the existence of the condition.

### Case report

A white woman, aged 28, was admitted to Whipps Cross Hospital on 5 September 1968, three weeks after the delivery of her first child. Four days before admission she developed severe central chest pain during moderate exertion; the pain lasted 15 minutes and was accompanied by dyspnoea. Since then she had been breathless on slight exertion. She had never previously had similar symptoms. Her routine antenatal examinations were normal, with no albuminuria and a blood pressure ranging between 110/80 and 130/80 mm. Hg. Her chest x-ray on 22 February 1968 was normal (Fig. 1). Artificial rupture of the membranes was performed on 12 August after a 43-week pregnancy; on the same day she developed a macular rash on her lower abdomen which spread over her body and subsided after two weeks. She was not given any drugs until after the onset of this rash. She had a normal baby girl, birthweight 3912 g., by forceps delivery on 14 August. Because her bladder had been catheterized three times during the delivery, she was given a prophylactic 5-day course of sulphadimidine 4 g. daily. She also had stilboestrol and, because of rhesus incompatibility, anti-D  $\gamma$ -globulin. She remained afebrile throughout the postnatal period and had no symptoms then or earlier of a viral or other infection.

Her past medical history was uneventful apart from the spontaneous abortion of a 12-week foetus when she was 26. She rarely drank alcohol. Her parents and six sibs were alive and well: there was no history of heart disease in them or any other members of the family.

**Clinical examination** On 6 September 1968 the patient was transferred to Brompton Hospital. She was found to be slightly dyspnoeic with peripheral vasoconstriction, blood pressure 110/70

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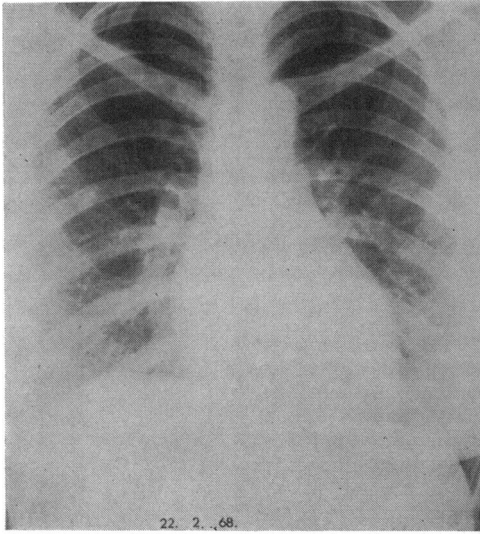


FIG. 1 Chest x-ray on 22 February 1968.  
Cardiothoracic ratio 12:26 cm.

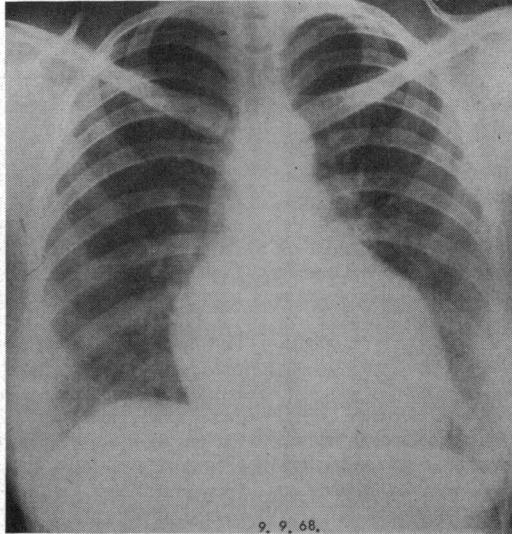


FIG. 3 Chest x-ray on 9 September 1968.  
Cardiothoracic ratio 15.5:25 cm.

mm. Hg, and sinus tachycardia. The jugular venous pressure was high (10 cm. above the sternal angle). There was a gallop sound and a normally split second heart sound with accentuation of the pulmonary component. There were no murmurs. Crepitations were audible at both lung bases. The rest of the examination was normal.

The electrocardiogram showed left axis deviation, low voltage QRS complexes, and inverted T waves in V<sub>2</sub>-V<sub>6</sub> (Fig. 2). The chest x-ray showed an increase in size of the heart compared with the previous film (Fig. 3).

Right heart catheterization showed a raised 'wedge' pressure, suggesting left ventricular failure, and raised pulmonary artery, right atrial, and right ventricular end-diastolic pressures, confirming right ventricular failure. The pul-

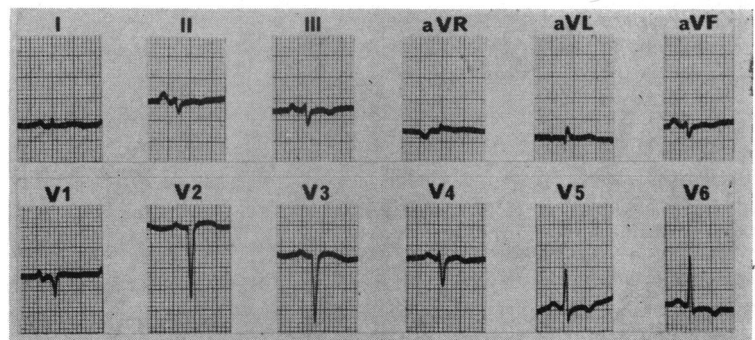
monary arterial oxygen saturation and cardiac output were low (Table). There was no evidence of pericardial effusion. Left heart catheterization and angiocardiology were not carried out because of the patient's condition.

**Investigations** Haemoglobin 14.6 g./100 ml. White blood cell count 9,700/cu. mm., with a normal differential count and film. Eosinophil count 390/cu. mm. ESR 2 mm. in first hour. Lupus erythematosus cells negative. Antinuclear factor negative. Rheumatoid factor negative. Myocardial immunofluorescent antibodies negative. Immunoglobulins normal (IgA 275 mg./100 ml., IgG 960 mg./100 ml., IgM 130 mg./100 ml.). Serum proteins: albumin 4.1 g./100 ml., globulin 2.9 g./100 ml.; electrophoresis normal. Cholesterol 240 mg./100 ml. Protein-bound

TABLE Right heart catheterization on  
6 September 1968

| Site   | Pressure (mm. Hg)              |      |
|--|--------------------------------|------|
|  | S/D                            | Mean |
| Right atrium                                     | a = 15 x = 10<br>v = 14 y = 11 | 13   |
| Right ventricle                                  | 43/9-16                        |      |
| Pulmonary artery                                 | 43/28                          | 34   |
| Pulmonary artery wedge                           | a = 28 x = 25<br>v = 34 y = 22 | 27   |
| Arterial oxygen saturation (assumed) 97 per cent |                                |      |
| Pulmonary arterial oxygen saturation 37 per cent |                                |      |
| AV oxygen difference = 13.4 ml./100 ml.          |                                |      |
| Oxygen uptake = 214 ml./min./sq. m.              |                                |      |
| Cardiac index = 1.6 l./min./sq. m.               |                                |      |

FIG. 2 Electrocardiogram on 9 September 1968.



iodine 6  $\mu\text{g.}/100\text{ ml.}$  Pyruvate tolerance test (on 1 October 1968): blood pyruvate - fasting 0.95 mg./100 ml., 60 minutes 1.4 mg./100 ml., 90 minutes 1.2 mg./100 ml. Glucose tolerance test (on 18 September): blood glucose, fasting 89 mg./100 ml., 120 minutes (after 50 g. oral glucose) 79 mg./100 ml. Enzymes on 7 September 1968: SGOT 26 Frankel Units/ml. (normal 5-40 U./ml.), SGPT 13 Frankel Units/ml. (normal 5-35 U./ml.), and LDH 500 U./ml. (normal 200-400 U./ml.). Blood cultures were sterile on 5 occasions. Stool cultures, no virus isolated in monkey kidney or HEP<sub>2</sub> tissue cultures or after 2 passages in suckling mice. Complement-fixation tests to influenza, adenovirus, respiratory syncytial virus, *Rickettsia burnetii*, psittacosis, and *Mycoplasma pneumoniae* negative, and to herpes simplex 1/40 on 9 and 23 September and 14 October. Coxsackie B<sub>1</sub>-B<sub>6</sub> neutralization tests on 14 October - less than 1/16. Antistreptolysin titre 50-200 U./ml. Wassermann reaction negative. Toxoplasma dye test negative.

**Progress** The clinical diagnosis of cardiomyopathy with biventricular failure was confirmed by catheterization, and the patient was treated with strict bed-rest, digoxin, and diuretics. After an initial slight improvement her condition progressively deteriorated. Thiamine and prophylactic oral anticoagulants were added to the regimen. By 19 October she had become breathless despite large doses of diuretics. Both steroids and later broad spectrum antibiotics were given. The steroids caused hyperglycaemia, which required insulin for its control, and after the introduction of antibiotics oral candidiasis developed. Neither treatment arrested the gradually increasing oedema and dyspnoea. The patient died on 2 December 1968.

**Necropsy** The heart weighed 480 g. The muscle was pale and flabby. The left ventricular wall thickness was 1.4 cm., the right 0.3 cm. All chambers of the heart were dilated. Both ventricles and the left atrium contained numerous fresh and organized mural thrombi. The valves and coronary arteries were normal. Microscopically the dominant feature was degeneration of the myocardial fibres. These varied conspicuously in size (Fig. 4). Most were atrophic, with loss of cross-striation, fragmentation, and rarefaction of the cytoplasm, and absent or small pyknotic nuclei. A few myocardial fibres were hypertrophied with abundant cytoplasm and hyperchromatic nuclei. There were small areas of myocytolysis and gradual replacement by fine bands of collagenous connective tissue. There were a few areas of acellular fibrosis (Fig. 5). Sparse lymphocytic infiltration occurred in a few small foci only. Extensive mural thrombosis was prominent; where mural thrombosis was absent, the endocardium was not thickened.

The lungs were congested and contained several nodules ranging from 4 cm. to 1 cm. in diameter: microscopically these were infarcts containing aspergillus hyphae. There were no thrombi or emboli in the pulmonary arteries or arterioles. The liver and spleen were conspicuously congested. The rest of the post-mortem examination including that of the brain was normal.

### Discussion

The present case fulfils the criteria for the diagnosis of peri-partum cardiomyopathy. The only aetiological factors that were difficult to exclude were thiamine deficiency and sulphonamide hypersensitivity. Malnutrition has been implicated as a cause of post-partum

FIG. 4 Section of myocardium showing variation in size of myocardial fibres, myocytolysis, and loss of nuclei. (H. and E.  $\times 315$ .)

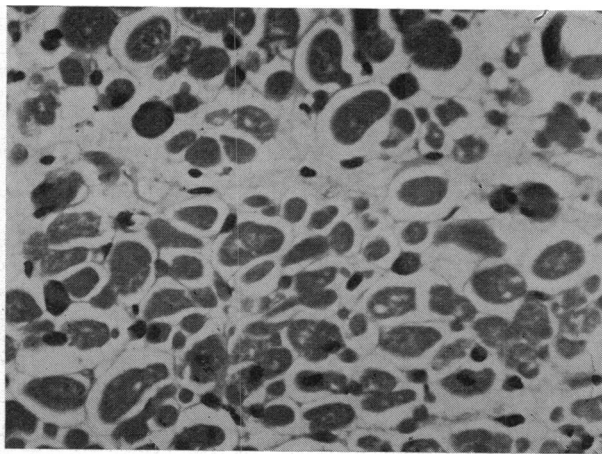
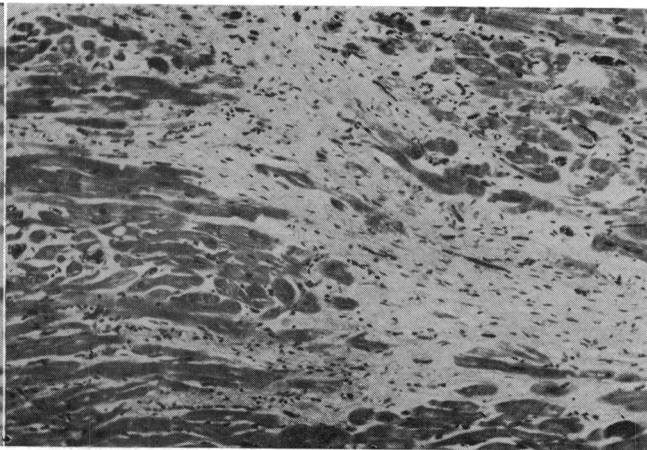


FIG. 5 Section of myocardium showing an area of acellular fibrosis. (H. and E.  $\times 87$ .)



heart disease in negroes (Seftel and Susser, 1961; Walsh *et al.*, 1965). In the present patient there were no clinical signs of thiamine deficiency, the cardiac output was low, and the pyruvate tolerance test was within the expected limits for a patient in congestive heart failure (Joiner, McArdle, and Thompson, 1950).

Bashour and Winchell (1954) described a patient who recovered from heart failure associated with left bundle-branch block presenting after the administration of sulphonamides in the puerperium. They considered that the heart failure could be attributed either to the post-partum state or to sulphonamides. In most other reports sulphonamide hypersensitivity myocarditis has either been an incidental finding at necropsy (French and Weller, 1942; Simon, 1943; Gore and Saphir, 1947) or has produced a transient episode of cardiac failure associated with a clinically obvious hypersensitivity reaction, a peripheral blood eosinophilia, and electrocardiographic evidence of conduction defects (Lilienfeld, Hochstein, and Weiss, 1950; MacSearraigh and Patel, 1968). Two cases of fatal heart failure following sulphonamide administration were described by Blanchard and Mertens (1958). Both patients had fever, but no other sign of hypersensitivity, both had coexisting ischaemic heart disease, and both, like all the other post-mortem cases of sulphonamide myocarditis, had an extensive eosinophilic infiltration of the myocardium. The present patient had no fever, no rash attributable to sulphonamide hypersensitivity, and no peripheral blood eosinophilia. The post-mortem appearance was unlike that of the previously described cases of sulphonamide myocarditis.

In our definition of peri-partum cardiomyopathy we have excluded cases of heart failure associated with pre-eclamptic toxæmia or eclampsia. This association has been frequently described (Szekely and Snaith, 1947; Benchimol *et al.*, 1959; Rosen, 1959; Tweed, 1960; Hunyadi-Buzás and Moret, 1966; Johnson *et al.*, 1966). It is not known whether the factor responsible for the myocardial damage is the same in the patients with pre-eclamptic toxæmia as in the patients with peri-partum cardiomyopathy.

Two cases of fatal cerebral infarction presenting with sudden loss of consciousness during pregnancy were found at necropsy to be associated with cardiomyopathy (Connor and Adams, 1966; Ledingham *et al.*, 1968). We do not regard these as proven cases of peri-partum cardiomyopathy because the myocardial damage may have been

secondary to the cerebral infarction. Connor (1968) has shown that cerebral infarction is not infrequently associated with focal myocardial degeneration.

Rare cases of rapidly progressive and fatal heart failure during pregnancy or the puerperium have been described in association with a post-mortem appearance of an acute inflammatory myocarditis (Mendelson, 1951; Faruque, 1965). Faruque (1965) made the attractive suggestion that peri-partum cardiomyopathy might be the result of an acute myocarditis which was asymptomatic and not identified in the acute stage.

Of the other cases of peri-partum cardiomyopathy, the present case closely resembles that of Muller and Bonard (1968) in clinical course, and morbid anatomical and histological findings. The case of Brown *et al.* (1967) differed in its presentation before delivery, persistent left bundle-branch block, and complete clinical recovery.

Brigden (1964; 1969, personal communication) and Brown *et al.* (1967) have suggested that some of the patients developing heart failure due to primary myocardial disease during or after pregnancy have pre-existing but hitherto unrecognized heart disease. Many of Brigden's cases were found on careful inquiry to have either a family history of heart disease, or evidence of asymptomatic heart disease from a previous medical examination, x-ray, or electrocardiogram. In our case, there was no family history, and no evidence of heart disease during her pregnancy.

The cause of peri-partum cardiomyopathy is unlikely to be elucidated until further cases have been described and their common features identified.

We would like to thank Dr. H. W. Balme, Whipps Cross Hospital, for referring the patient, and Dr. M. H. Lessof, Guy's Hospital, for the myocardial antibody and immunoglobulin estimations.

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